

Remarks/Arguments

Prior to the present amendments, claims 12-14 were pending in this application and stood rejected. Claims 13 and 15 have been canceled and claim 12 has been amended. The amendment of claim 12 is incorporation of subject matter originally recited in claim 13. All amendments and cancellations were made without prejudice or disclaimer. Applicants explicitly reserve the right to pursue any deleted subject matter in one or more continuing applications.

Rejection Withdrawn

Applicants note and appreciate the withdrawal of the rejection of claims 12-14 under 35 U.S.C. 101, and the acknowledgement that the mixed lymphocyte reaction (MLR) assay is an art accepted assay for identifying immune suppressive molecules and is generally predictive of their *in vivo* effectiveness.

Claim Rejections – 35 U.S.C. § 112, First Paragraph, Enablement

Claims 12-14 have been rejected under 35 U.S.C. 112, first paragraph as allegedly failing to comply with the enablement requirement.

According to the rejection: “[i]t is unclear how the results of the MLR assay relate to the claimed invention.” (Office Action, page 4, emphasis omitted.) In fact, from the subsequent analysis, it appears that the Examiner takes the position that the combined results of the MLR assay and the vascular permeability assay disclosed in the present application do not enable the rejected claims.

Citing Haskill et al., U.S. Patent No. 5,817,306 for the teaching that the MLR assay is valuable for identifying immune suppressive molecules *in vitro* that are useful for treating graft versus host disease, Coleman et al. U.S. Patent No. 5,780,268 for its teaching that investigation of MLR assays have provided information on graft rejection and its suppression and contributed to the understanding of the multiplicity of phenotypes that are important for histocompatibility, the Examiner acknowledges the value of the MLR assay. In contrast, with regard to the vascular permeability (Miles) assay the Examiner cites Yeo et al. (of record) in support of the assertion that the results of the Miles assay are preliminary, and, absent further validation, may be due to false-positives.

From this analysis, the Examiner concludes that the combined results obtained in the two assays are “not tantamount to an effective method of enhancing the infiltration of (any type of) immune cells (in any type of disease or condition) and/or alleviating any type of infection in a mammal.” (Office Action, paragraph bridging pages 5 and 6) The Examiner further notes that the claimed invention would not predictably function for the broad purpose of alleviating diverse infections such as STDs, tuberculosis, pink eye, bronchitis, etc., and does not correlate to use of the claimed protein in a therapeutically effective manner for the breadth of the rejected claims.

The Examiner concludes that undue experimentation would be required to practice the invention to enhance the infiltration of *any type* of immune cell, in *any type of disease/conditions* and/or to alleviate *any type of infection*.

Without acquiescence to the Examiner’s position and solely to simplify the issued under consideration and thus expedite prosecution, claims 13 and 14 have been canceled, which moots their rejection. The rejection of claim 12 is respectfully traversed.

As a result of the cancellation of claim 14, the Examiner’s comments on the scope of infections to be treated in accordance with the present invention no longer apply, and thus will not be addressed herein.

Claim 12 now recites a method of enhancing the infiltration of immune cells in a mammal, comprising administering to the mammal an effective amount of Bolekine polypeptide as shown in Figure 2 (SEQ ID NO: 2), wherein the immune cells are mononuclear cells, eosinophils, or polymorphonuclear neutrophils (PMNs). The claim is drawn to enhancing the infiltration of immune cells for which the specification provides actual experimental data, thus its scope is fully supported by the disclosure of the present application. In addressing the alleged limitations of the Miles assay, Applicants refer to the expert Declaration of Dr. Fong (of record), the fact, statements and conclusions of which have not been effectively rebutted by the Examiner. While Baggiolini et al., referred to in the Declaration, may not teach that “any one chemokine can enhance the infiltration of all immune cells (in any type of disease or condition) and/or alleviate any type of infection in a mammal,” this is irrelevant in view of the current claim scope. Based on its primary structure, Bolekine has been unquestionably identified as a novel chemokine. Thus, based on general knowledge in the art that several chemokines are known to activate immune cells, one of ordinary skill would accept the data disclosed in the present

application a valid, and would be able to practice the invention within the full scope of pending claim 12 without undue experimentation.

In addressing the post published evidence submitted by Applicants, the Examiner notes that applicants have not provided :a sequence alignment, which demonstrates that the instant Bolekine polypeptide (SEQ ID NO: 2) is indeed CXCL14/BRAK.” (Office Action, page 12). The attached entry from NCBI Genbank clearly establishes that CXCL14, BRAK and Bolekine are synonyms for the same chemokine. Indeed, the sequence of Bolekine is accessible under the same accession number (NP_004878) as that of BRAK and CXCL14. As far as the Examiner’s comments on the post published references are concerned, claim 12 pending is not directed to the enhancement of “any type” of immune cell or the treatment of “any type” of disease or infection. Accordingly, the scope of claim 12 is entirely commensurate with the specific teaching provided in the present application, when read by one skilled in the art, taking into account the general knowledge in the art at the time the present invention was made.


Finally, it is noted that absolute certainty is not required for patentability, and even extensive experimentation is permissible, as long as it is routine in nature. Thus, when applying the correct legal standard, one should arrive to the conclusion that the invention claimed in the present application is fully enabled, and the present rejection should be withdrawn.

All claims pending in this application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, or credit overpayment to Deposit Account No. **50-4634**
(referencing Attorney's Docket No. 123851-181880 (**GNE-1192-2**)).

Respectfully submitted,

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